LARGE SCALE PRODUCTION AND PROPERTIES OF HUMAN LEUKOCYTE INTERFERON USED IN CLINICAL TRIALS

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INTRODUCTION

Human leukocyte interferon has been produced for clinical use in our laboratories for several years (1). A routine procedure for the production and purification has been established (2,3), but studies to improve the recovery and quality of the clinical interferon continue. Since the availability of fresh leukocytes is the factor limiting production, maximization of the interferon yield per blood unit is of prime importance.

In clinical trials with interferons some side-effects including pyrogenicity have appeared. These have prompted us to analyse the impurities of the interferon preparations to see whether the side-effects could be eliminated by further purification. This paper describes our recent studies on the production of the human leukocyte interferon for clinical use and on the properties of the interferon preparations employed in the current clinical trials.

PRODUCTION

Storage of Blood

Routinely, only buffy coats from fresh blood are collected. In practice the collection takes place 2-5 hours after donation. The buffy coats are stored overnight at 4°C and used the next day for interferon production. If production is started immediately after harvesting the cells, the interferon titers are only slightly higher. If the buffy coats are harvested from one-day-old blood and in addition stored overnight so that the total storage time is two
days, the interferon titers are clearly reduced. With additional storage the titers are reduced further (Fig. 1).

![Graph showing interferon production over days of storage.](image)

**Figure 1**

Production of interferon by leukocytes stored for different periods of time at 4°C.

When the blood is stored before harvesting the buffy coat, the leukocytes separate in centrifugation as a more distinct layer and more leukocytes can be recovered from the same volume. The maximum yield of leukocytes counted after purification of the cells is gained when the blood is stored for one day before harvesting.